

## **REMARKS**

With entry of this amendment, claims 1, 4, 5, 8, 11-16, and 18 are pending. Applicants have canceled claims 3, 6, 7, 9, 10, and 20-24 without prejudice or disclaimer of the subject matter of those claims. Applicants have also amended claims 1 and 16 to specify that the at least one purine nucleic acid-related substance is chosen from adenosine phosphate and salts of adenosine phosphate and that the at least one pyrimidine nucleic acid-related substance is chosen from uridine monophosphate and salts of uridine monophosphate. The specification supports this amendment at, for example, page 7, lines 29-31; page 8, lines 11-14 and 23-26; page 9, lines 32 and 33; and page 10, lines 10-12. These amendments therefore do not introduce new matter.

### **Rejections Under 35 U.S.C. §§ 101 and 112**

The Office rejects claims 21 and 22 under 35 U.S.C. §§ 101 and 112, second paragraph, because these claims allegedly contain an "improper definition of a process" and do "not set forth any steps involved in the method/process." Office Action, page 2. Solely to advance prosecution and without acquiescing in this rejection, Applicants have canceled claims 21 and 22. Because this rejection is now moot, Applicants request that the Office withdraw it.

### **Rejection Under 35 U.S.C. § 103**

Claims 1, 3-16, 18, and 20-24 stand rejected under 35 U.S.C. § 103 as allegedly obvious over Croucher et al. (*Biochimica et Biophysica Acta*, 1502:297-306 (2000); "Croucher"). *Id.* at 3. According to the Office, Croucher teaches that "adenosine triphosphate and uridine triphosphate in the presence of serum increased sulphated glycosaminoglycan and collagen deposition above control levels." *Id.* at 4. Acknowledging that Croucher does not teach a composition containing both ATP and

UTP, the Office nonetheless believes that it “would have been obvious . . . to combine ATP and UTP to increase collagen production.” *Id.* In alleged support for this rejection, the Office suggests that “[u]se of materials in combination, each of which is known to function for [an] intended purpose, is generally held to be prima facie obvious. . . .” *Id.*

Finally, the Office also contends that, though Croucher does not teach monophosphate derivatives of ATP and UTP, which are at issue here, “the skilled artisan would have had a reasonable expectation of success by using the corresponding monophosphate derivatives.” *Id.* Applicants respectfully disagree and address this rejection with respect to claims 1, 4, 5, 8, 11-16, and 18, which are still pending.

Solely to advance prosecution, Applicants have amended claims 1 and 16 to recite “at least one purine nucleic acid-related substance and at least one pyrimidine nucleic acid-related substance, wherein the purine nucleic acid-related substance is chosen from adenosine phosphate and salts of adenosine phosphate and wherein the pyrimidine nucleic acid-related substance is chosen from uridine monophosphate and salts of uridine monophosphate.” According to the Office’s description of Croucher, this reference only teaches the use of uridine triphosphate (“UTP”) and contains absolutely no teaching on the use of a uridine monophosphate (“UMP”). Despite this, the Office simply asserts that the skilled artisan would have a reasonable expectation of success in using monophosphate derivatives without providing any reason or proof to support this contention. As Applicants will explain, the Office’s assumption is incorrect.

The specification clearly shows that when a uridine monophosphate is used alone, no increase in collagen production occurs. As shown in Test Example 2 at pages 17 and 18 along with Table 1 and Figure 2, adding a UMP alone to fibroblast media

resulted in procollagen type I C peptide ("PICP") production no different from control media without any nucleotide phosphate. See Figure 2, compare test medium 3 and test medium 4. In other words, a UMP alone resulted in no collagen production. Croucher, on the other hand, suggests that UTP alone does promote collagen production. The results suggest that pyrimidine compounds function differently from one another and are not interchangeable as the Office seems to assert.

Returning to Test Example 2, the inventors not only measured the effect of a UMP alone on PICP production by human skin fibroblasts and the effect of an adenosine phosphate alone on PICP production in these cells, they also measured the effect of a UMP and an adenosine phosphate together on PICP production. Applying an adenosine phosphate alone to skin fibroblasts resulted in an increase in PICP production over that seen in the negative control and the UMP sample. See *id.*, compare test medium 2 to test media 3 and 4. Moreover, unexpectedly, adding a UMP to an adenosine phosphate significantly increased the amount of PICP made by fibroblasts compared to the adenosine phosphate alone. See *id.*, compare test medium 1 to test medium 2. Thus, absent the specification's showing of synergy between an adenosine phosphate and a UMP, one of ordinary skill in the art would not have had a reasonable expectation of success in using UMP to stimulate collagen production. Indeed, Croucher's teaching in no way hints at the combined effect or even the additive effect of an adenosine phosphate and a UMP used together. In sum, given that a UMP on its own did not promote collagen production, it would not have been obvious at the time of the invention to use a UMP in any composition to promote collagen production.

In addition, regarding method claims 16 and 18, Croucher does not teach the step of "applying to the skin." Instead, Croucher used its compositions on

chondrocytes, which are not cells found in the skin. Moreover, Croucher teaches that some nucleotides can have different effects on different types of chondrocytes. See page 298, left column. Given that nucleotides can have different effects on the same cell type (i.e., chondrocytes) taken from different sources such as arteries or the nose, one of ordinary skill in the art would have had no reason to believe that ATP or UTP would produce the same effect in skin cells as in chondrocytes, let alone what UMP and, for example, AMP might do. Thus, based on the teaching of Croucher, the methods of claims 16 and 18 would not have been obvious. Applicants therefore request that the Office withdraw its rejection of claims 1, 3-16, 18, and 20-24.

#### Conclusions

In view of the foregoing amendments and remarks, Applicants respectfully request reconsideration and reexamination of this application and the timely allowance of claims 1, 4, 5, 8, 11-16, and 18.

Please grant any extensions of time required to enter this response and charge any additional required fees to Deposit Account No. 06-0916.

Respectfully submitted,

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